Introduction and Cardiac Automaticity

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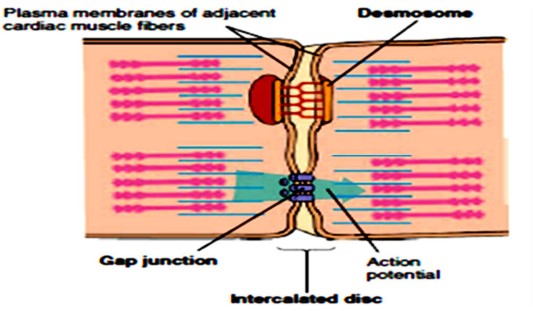
ILOs:

By the end of this lecture the student should be able to:

- Describe the functional parts of the cardiovascular system
- List the site of initiation and propagation of the cardiac action potential
- Explain why the SAN is the cardiac pacemaker specifications
- List which ion modulates the phases of the ventricular and pacemaker action potentials
- Compare fast- and slow response action potentials

Cardiac muscle is a syncytium

- The heart is not a true syncytium but acts as a functional syncytium, as regards its electrical and mechanical functions. This is attributed to the junctions found at the intercalated discs which are:
    - Gap junctions
      Allow high electric conduction with low resistance, thus providing the spread of excitation from one cell to another all over the cardiac muscle (electrical syncytium).
    - Desmosomes
      Act as tight junctions. When one of the adjacent cells contracts, it pulls on the other causing the heart to contract as one unit leading to more efficient pumping force (mechanical syncytium).
- The heart is composed of 2 functional syncytia:
  atrium syncytium which constitutes the wall of 2 atria and ventricular syncytium which constitutes the wall of 2 ventricles. This allows the atria to contract short time before the ventricular contraction, which is important for effectiveness of heart pumping. Thus, the ventricles can receive blood from the atria during atrial systole.



Intercalated disc

Types of Heart Cells

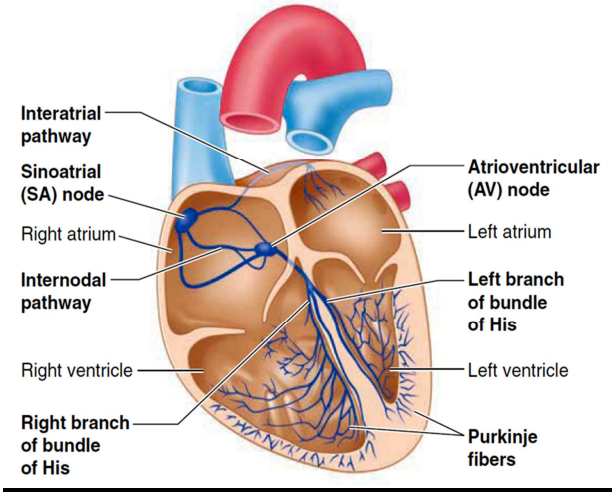
The heart contains 2 types of cells

1. Contractile cells

- Form 99% of the cells.
- These form atrial and ventricular walls.
- They do mechanical work of pumping but normally they do not initiate their own action potential.

2. Autorrhythmic cells

- They make up about 1% of cardiac muscle cells.
- They constitute a network known as conducting system of the heart and are in contact with the contractile fibers via gap junctions.
- The autorrhythmic cells do not contract but are specialized for initiating and conducting the action potentials responsible for contraction of the working cells.
- The cardiac autorrhythmic cells are:
    - Sinoatrial node (SAN)
    - Atrioventricular node (AVN)
    - Bundle of His (atrioventricular bundle)
    - Right and left bundle branches
    - Purkinje fibers



Cardiac autorrhythmic cells

Properties of the Cardiac muscle

- Auto-rhythmicity (Automaticity and rhythmicity)
- Excitability
- Conductivity
- Contractility

Automaticity and rhythmicity (Auto-rhythmicity)

Automaticity

It is the property of self excitation

It is the ability of heart to initiate its own beat = ability of certain cardiac cells "pace maker" to spontaneously depolarize and generate action potential

Rhythmicity

Is ability to continue beating regularly i.e. at a rhythm

The SAN is the normal pacemaker of the human heart as it is specialized in initiation of the action potential with the highest frequency (most rapidly = 100 action potentials per minute) at a regular rhythm.

The rate of discharge of SAN determines the rate at which the heart beats. This is called **normal sinus rhythm, NSR.** (= SAN exhibits a spontaneous depolarization that causes action potentials, resulting in the automatic beating of the heart).

The normal heart rate, however, is about 70 bpm because SAN is under influence of vagal tone.
The rest of autorrhythmic cells form a specialized conductive system for conduction of the excitation wave to the rest of the heart as fast as possible.
The various parts of the conduction system are capable of spontaneous discharge. But, they are normally suppressed by action potentials originating in the SAN as the SA node normally discharges most rapidly, with depolarization spreading from it to the other regions before they discharge spontaneously.

The AVN is considered secondary pacemaker and have normal rate of discharge 40-60 bpm while Purkinje fibers is the tertiary pacemaker 15-40 bpm
The pace maker tissue is self- excitable, while the contractile and conductive tissues only respond when stimulated by impulses coming from the pacemaker.

Why is the SAN the cardiac pacemaker?
SAN is the most self excitable part because:

- Its RMP is lowest in magnitude (-55 mV)
- It has most unstable RMP with highest slope
    - During the period of diastole, SAN exhibits a slow spontaneous depolarization called pacemaker potential.
    - Because this pacemaker potential occurs during diastole, it is also called a diastolic depolarization.
- It reaches to threshold of firing (- 40 mV) in shortest time

Electrical Activity of the Heart

Cardiac Action Potentials

Two types of action potentials may be recorded from cardiac cells

I. Fast response action potential
II. Slow response action potential

The cardiac muscle fibers can be divided into 2 types:

- Fast response fibers
- Slow response fibers

Fast response fibers

- Maintained RMP
- Fast AP

These fibers are present in:

- contractile tissue as the muscle cells in atria and ventricles
- junctional tissue as the His bundle, bundle branches and Purkinje fibers.

Slow response fibers

- Unstable RMP
- Slow AP

These fibers are present in pacemaker tissue in SAN and AVN

Fast Response Action Potential

Characteristics and ionic basis

Resting membrane potential (RMP) (phase 4)

It is the potential difference between outside and inside of the cell membrane during the resting state.

- In the contractile tissue such as ventricular fibers, the RMP is stable.
- Its magnitude is high (about -90 mv).
- The stable RMP in the fast fibers is due to an outward leak of K^+ current (K^+efflux through leaky K^+channels)

Depolarization: (Phase 0 = Upstroke = rapid depolarization)

- When the fast fibers are stimulated by an excitation wave, it shows a rapid rising depolarization and the membrane potential rapidly reverses to a positive value of about +20 mV (reversal of polarity = overshoot).
- This phase is caused by increased membrane Na^+ permeability and rapid influx of Na^+ due to opening of the voltage-gated fast Na^+ channels.

– Activation of the fast Na^+ channels starts immediately by the decrease of the potential difference from -90 mv till reaching to a threshold of -70 mV, which opens fully the activation gate (m) of the fast Na^+ channels.

Repolarization:

It is triphasic:

Initial repolarization (phase 1)

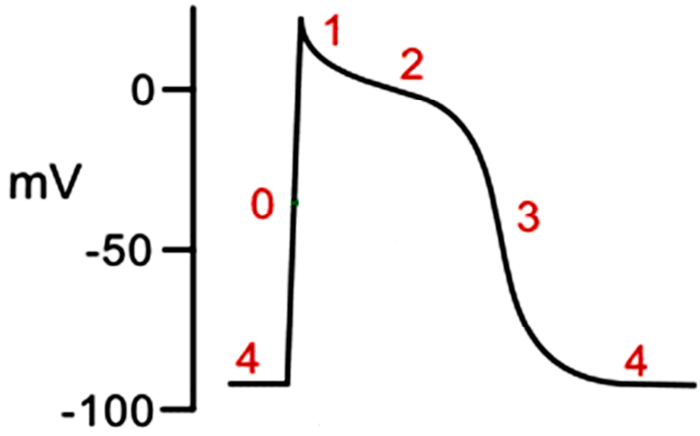
– It is due to inactivation of Na channels and K^+ efflux due to opening of the transient voltage gated K^+ channels.

Plateau (phase 2)

- It is due to opening of the slow voltage gated Ca^{++} channels (L-type) (slow but prolonged opening).
- The almost equal slow Ca^{++} influx through the slow voltage gated Ca^{++} channels (L-type) and the slow efflux of K^+ outside the cell causes the membrane potential to be maintained near zero mv.
- It lasts for a prolonged period of about 200-300 msec.

Rapid repolarization (phase 3)

- It is due to closure of the slow Ca^{++} channels and increased potassium permeability and rapid efflux of K^+ due to opening of the voltage gated K^+ channels and the cell membrane potential returns to its resting level.



Fast response action potential

The action potential is brought back to the RMP or **Phase 4**. The sodium-potassium ATP-ase is responsible for the maintenance of RMP until the arrival of the next action potential.

Restoration of electrolytes

- Na^+-K^+- ATPase pump restores the small changes in [Na^+] and [K^+]
- Most of Ca^{2+} that enter the cell are pumped out by Na/Ca exchanger (pumps 3 Na^+ inside for 1 Ca^{2+}outside the cell)
- A small fraction is pumped out by Ca^{2+}- ATPase pump

Slow Response Action Potential

Characteristics and ionic basis

Resting membrane potential (RMP) (phase 4)= pacemaker potential

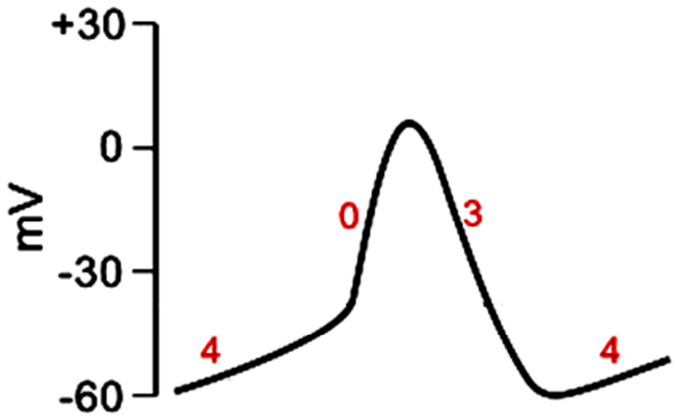
- The RMP of the pace maker tissue is characterized by:
    - having a lower magnitude (- 55 to - 60 mv)
    - being unstable with an upward slope which is called prepotential (also called diastolic depolarization) = it shows slow spontaneous depolarization which occurs during diastole .
- The instability of the RMP that gives rise to an upward slope is due to progressive accumulation of positive charges inside the pacemaker cells, which is caused by the imbalance between the more active inward ion (Na^+ and Ca^{++}) currents, and the weak outward K^+ current (due to progressive closure of potassium channels).
- At the end of repolarization, when the membrane potential is very negative (about -60 mV), a voltage gated channel permeable to Na^+ is activated. Because this channel is activated following hyperpolarization, when the potential becomes more negative at the end of repolarization from the previous action potential, they are called **funny,** or $\mathbf{I_f}$ channels or $\mathbf{I_h}$ channels.
- The slow continuous Na^+ influx (inward Na^+ current) through these channels causes the membrane to begin to depolarize, forming the first part of the prepotential and causes the membrane potential to decrease spontaneously from -60 mV to - 50 mV.
- When the membrane potential reaches -50 mV, transient, T-type Ca^{++} channels open causing calcium influx which completes the prepotential and brings the membrane potential to firing level (-40 mV).

Depolarization (phase 0)

- Depolarization is due to:
    - influx of Ca^{++} through the slow Ca^{++} channels (long-lasting, L-type), which are open at the threshold of firing (-40 mv).
    - The upstroke (phase 0): has a low magnitude (about 60 mv) and takes more time to reach its peak.

Repolarization (phase 3)

- Is monophasic and gradual.
- Is due to K^+ efflux that occurs when K^+ permeability increases due to activation of voltage gated K^+ channels, coupled with closure of the L-type Ca^{++} channels.



Slow response action potential

Effects of autonomic nerves on pace maker potential

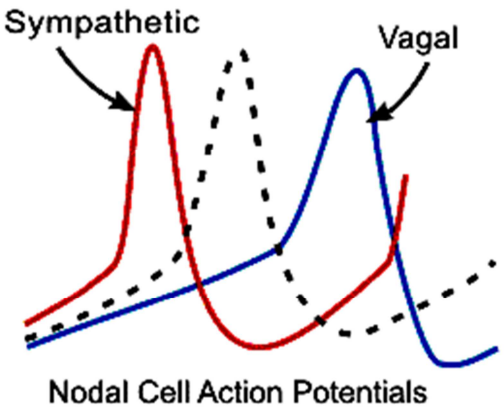
Sympathetic nerves

- Release norepinephrine which binds to $\beta_1$adrenergic receptors and increases the heart rate by production of more action potentials per unit time by increasing intracellular cAMP which:
    - opens $\mathbf{I_h}$ channels for Na^+, increasing Na^+ influx which increases the rate of diastolic depolarization (higher slope), thus the threshold potential is reached more quickly.
    - Facilitates the opening of L-Ca^{++} channels, increasing the influx of Ca^{++} and hence more rapid upstroke of action potential

(phase 0 occurs faster).

Parasympathetic nerves

- Release acetylcholine, which binds to M_2 muscarinic cholinergic receptors and decreases the heart rate by production of less action potentials per unit time by:
    - Opening of K^+ channels resulting in an enhanced K^+ efflux which decreases rate of diastolic depolarization and causes lower slope.
    - Decreasing intracellular cAMP which slows the opening of Ca^{++} channels, results in a decrease in the firing rate of action potential (phase 0 occurs later).



Effect of sympathetic and parasympathetic stimulation on slow response action potential